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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,487	10/21/2003	Sakari Kauppinen	50287/007002	8760

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EXAMINER	
WOLLENBERGER, LOUIS V	
ART UNIT	**PAPER NUMBER**
1635	

NOTIFICATION DATE	DELIVERY MODE
11/15/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/690,487	KAUPPINEN ET AL.	
	Examiner	Art Unit	
	Louis V. Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2007 and 04 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-86,157-159 and 185* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,22-24,32-34,36,42-46,51-55,72,74-76,80-83 and 157* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/20/04; 12/8/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-17,20,21,25-31,35,37-41,47-49,56-71,73,77-79,84-86,158,159 and 185.

DETAILED ACTION

Election/Restrictions/Status

Applicant's election without traverse of the population recited in part xiii of claim 157 in the reply filed on 9/18/2007 is acknowledged. Applicant states claims 18, 22-24, 32-34, 36, 42-46, 50-55, 72, 74-76, and 80-83 read on the elected invention.

In a telephone conversation held with Attorney for Applicant, Kristina Bieker-Brady, on 11/5/2007, the Examiner pointed out that claims 50 and 51 recited molecules with mutually exclusive features and that Applicant was required to elect one molecule thereof for prosecution. Attorney, on behalf of Applicant, elected the nucleic acid of claim 51.

In the reply filed 12/4/2006, Applicant elected Group IV, claims 157-159, drawn to methods of inhibiting gene expression using non-naturally occurring nucleic acids.

Altogether, then, Applicant's elected invention is considered to read on claims 18, 22-24, 32-34, 36, 42-46, 51-55, 72, 74-76, 80-83, and 157.

Claims 1-86, 157-159, and 185 are pending.

Claims 1-17, 20, 21, 25-31, 35, 37-41, 47-49, 56-71, 73, 77-79, 84-86, 158, 159, and 185 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the replies filed on 12/4/2006 and 9/18/2007.

Claims 18, 22-24, 32-34, 36, 42-46, 51-55, 72, 74-76, 80-83, and 157 are examined herein.

Specification/Sequence Compliance

The disclosure is objected to because of the following: This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The specification as filed does not comply with the requirements above, in particular 1.821(d) at least, because it contains nucleotide sequences of over 10 nucleobases each that are not identified by accompanying sequence identifiers.

For example, the sequences set forth at pages 240 *et seq* and at pages 252 and 254 of the specification and Fig. 17 of the drawings. This is but a sampling of the many sequences set forth in the instant application without SEQ ID NO: identifiers. Applicants are advised to review the entire application—claims, drawings, and specification—for complete compliance with the Sequence Rules.

Thus, the Examiner notes herein that the above listing of pages and figures which set forth examples in the specification of nucleotide sequences that require SEQ ID NO: is by way of illustration. In order to be fully responsive to this Office Action, Applicant should review this application in its entirety to ensure compliance with the requirements of 37 CFR 1.821 through 1.825 and to make all appropriate corrections.

Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 80-83 and 157 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 35-44 of copending Application No. 10/527211. Although the conflicting claims are not identical, they are not patentably distinct from each other because conflicting application 10/527211 claims a method for detecting the presence of one or more target nucleic acids in a sample, said method comprising (a) incubating said sample comprising said one or more target nucleic acids with a population of nucleic acids comprising at least one LNA oligomer, bonded to a solid support, under conditions that allow at least one of said target nucleic acids to hybridize to at least one of the nucleic acids in said population of nucleic acids. The LNA-comprising population may be any of those defined in claims 1-40, specific embodiments of which include LNAs having 2'-4'

O-C methylene bridges. The term "population" as defined at page 15 of the specification therein renders obvious the embodiments specifically recited in instant claims 82 and 83.

Therefore, one of ordinary skill in the art would conclude that the invention defined in the claims at issue is anticipated by, or would have been an obvious variation of, the invention defined in the claims in the conflicting application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 80-83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Factors to be considered in a determination of lack of enablement include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

The claims are drawn to a method of inhibiting gene expression, comprising contacting a cell with a population of LNA-comprising nucleic acids, wherein the populations is covalently bound to a solid support in an amount sufficient to attenuate the expression of a target nucleic acid. Claims 81-83 require the population be in a defined arrangement and comprise at least 10 or 100 different nucleic acids.

Thus, claims 80-83 are drawn to an array of nucleic acids, wherein members of the nucleic acid population are covalently bound to a solid support at discrete locations.

Adequate support does not exist in the instant application enabling one of skill to inhibit gene expression in one or more cells using an array of covalently bound nucleic acids. Rather, claims 80-83 would appear to be directed to an entirely different invention, a method for detecting and quantifying the expression of multiple genes simultaneously—i.e., a method of profiling gene expression, akin to microarray analysis.

Working examples and guidance in the specification teaching one of skill how to contact cells and inhibit gene expression in such cells using an array of covalently bound nucleic acids is not found in the instant specification. Not one instance, prophetic or otherwise, is found in either the prior art or the instant application showing the steps and materials necessary to practice the

instant method as now claimed. The method itself does not follow conventional, art-accepted practice for the introduction of naked or vector-encoded nucleic acid inhibitors—antisense, ribozymes, or siRNAs—into cells in culture or in vivo, and in the absence of such guidance, one of skill would be required to engage in undue experimentation to practice the method to the degree commensurate in scope with the claims.

A review of the instant 257-page application (for example, Examples 1, page 75, and Examples 5-13, beginning at page 92) shows the use of LNA-containing, array-bound probes for gene expression analysis. Therefore, one of skill would understand and be taught from the specification that Applicants contemplate using LNA oligomers for hybridization-based techniques of gene expression analysis, as in a conventional microarray-type analysis to detect the relative levels of multiple different genes in cells and tissues. This much is clear. However, it is not clear how such arrays are to be used to inhibit gene expression. Demonstration that multiple different covalently probes could be used to inhibit multiple genes following contact with cells is not found.

The state of the prior art teaches the use of arrays for measuring gene expression but not for inhibiting gene expression in the manner recited in the claims.

Thus, considering the breadth of the claims, the state of the art at the time of filing, the level of unpredictability in the art, and the limited guidance and working examples provided by the instant application, the Examiner submits that the skilled artisan would be required to conduct undue, trial and error experimentation to practice the claimed invention commensurate with the claims scope.

Accordingly, the instant claims are rejected for failing to comply with the enablement requirement.

Applicant is advised that should applicant amend claims 80-83 to include a new preamble claiming the instant embodiments for use in a method of detecting gene expression or the like, the claims will be withdrawn from further consideration as the claimed methods—steps and material limitations—would be considered to be distinct from the elected method drawn to a method of inhibiting gene expression.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18, 22-24, 32-34, 36, 42-46, 51-55, 72, 74-76, and 157 rejected under 35 U.S.C. 103(a) as being unpatentable over Orum et al. (US 2002/0068709 A1), Wahlestedt et al. (WO 01/25248), and Morgan et al. (1993) *Nucleic Acids Res.* 21:4615–4620.

With regard to the instantly claimed invention as a whole, including claim 74, Orum et al. taught antisense oligonucleotides having LNA and non-LNA segments for inhibiting gene expression in cells in vitro and in vivo. See Summary of the Invention at paragraphs 10-21. At paragraph it is taught an LNA-modified olignonucleotide contains one or more units of an LNA monomer, preferably one or more 2'-O, 4'-C-methylene bridge monomers. Methods for synthesis are taught, for example, at paragraph 75.

With regard to claims 22-24, Orum et al. taught antisense compounds of their invention have lengths in the range of about 12 to 40 nucleotides. More preferably 30 nucleotides; and most preferably about 12 to 20 nucleotides (paragraph 77). See also paragraphs 17 and 66, describing length recommendations.

With regard to claims 32-34, 36, 42-46, 51, 52, and 75, Orum et al. taught LNA-modified oligonucleotides preferably contain less than 70%, more preferably less than 60%, most preferably less than 50% LNA monomers and that their sizes are between 10 and 25 nucleotides,

more preferably between 12 and 20 nucleotides (paragraph 66); that incorporation of LNA monomers into a standard DNA or RNA oligonuclotide will increase its resistance towards nucleases (endonucleases and exonucleases), the extent of which will depend on the number of LNA monomers used and their position in the oligonucleotide (parag. 70); that an LNA-modified olignonucleotide contains one or more units of an LNA monomer, preferably one or more 2'-O, 4'-C-methylene bridge monomers (oxy-LNA) (parag. 16); that the LNA-modified oligonucleotide can be fully modified with LNA (i.e. each nucleotide is an LNA unit), but it is generally preferred that the LNA-modified oligomers will contain other residues such as native DNA monomers, or analogs thereof (parag. 16); and that in general, an LNA-modified oligonucleotide will contain at least about 5, 10, 15 or 20 percent LNA units, based on total nucleotides of the oligonucleotide, more typically at least about 20, 25, 30, 40, 50, 60, 70, 80 or 90 percent LNA units, based on total bases of the oligonucleotide (parag. 16).

Further with regard to claims 32-34, 36, 42-46, 51, 52, and 75, Wahlestedt et al. taught chimeric antisense oligonucleotides of varying lengths, comprising varying percentages of LNA and non-LNA monomers, such as DNA and RNA, in various combinations and in various patterns, including such embodiments wherein the LNAs are contiguous and alternating, central and flanking. It is said the LNA units may be at almost any position in the molecule to obtain the desired activity and/or affinity. See pages 1-14, especially pages 6-9, for example, page 8, lines 1-30.

With regard to claims 53-55 and 76, the instant claims are considered to recite inherent properties of the claimed LNA-containing nucleic acids, and specific species thereof, which nucleic acids, along with their inherent properties, are disclosed and suggested by the prior art.

Additionally, these aspects and properties of LNA-containing oligomers were recognized and taught by the prior art, as evidenced by Wahlestedt et al., who taught that the ability of an oxy-LNA oligo to discriminate between a complementary target RNA and a single base mismatched target RNA can be enhanced by incorporating non-oxy-LNA monomer (s), such as for instance DNA, RNA, thio-LNA or amino-LNA, either at, or close to, the mismatched position, and that oxy-LNA/non-oxy-LNA oligos may be selected on the basis of their increased specificity but unaltered RNAseH recruiting characteristics compared to the corresponding all oxy-LNA oligo (page 9, middle paragraph). mRNA splice variants are simply another variant form of wild-type mRNA. With regard to claim 76, Given that the prior art discloses LNA-containing nucleic acids with the structural features now recited for use in the method, it is submitted the disclosed LNA nucleic acids necessarily possess the functional/biochemical features recited in the claims. Burden is shifted to the Applicant to prove otherwise (MPEP §2112, citing *In re Best*: "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product). Orum et al. taught methods for determining target site accessibility and hybridization affinities and stabilities using melting temperature analysis (parag. 79-80). The significance of such information and ability to carry out such techniques are therefore within the knowledge of the skilled artisan.

With regard to claim 72, reciting a negative limitation, neither Orum et al. nor Wahlstedt et al. specifically require nor exclude 5-nitroindole.

Finally, with regard to claim 57, part xiii, Orum et al. taught LNA modified antisense oligonucleotides may be used in combinations. For instance, a cocktail of several different LNA modified oligonucleotides, directed against different regions of the same gene, may be

administered simultaneously or separately (paragr. 51 and 60). While silent as to whether the target sites are in one exon or another, it would be obvious to one of skill that all possibilities are inherently contemplated therein, and that any sites accessible to antisense would be candidates for inhibition.

Further with regard to claim 157, part xiii, the base claim, The prior art is replete with reports teaching methods for using combinations, i.e., pools or mixtures, of antisense oligonucleotides to target multiple sites in a single gene or multiple sites in different genes in cells *in vitro* and *in vivo*.

For instance, Morgan et al. (1993) *Nucleic Acids Res.* 21:4615–4620 teach the use of mixtures of antisense oligonucleotides to target multiple regions in a gene (see Abstract, page 4615; Results, pp. 4616-4619; and Discussion, page 4619). It is taught that such mixtures degrade mRNA targets more efficiently than many single oligos alone. It is taught that as a consequence of the improved potency, lower doses of oligos can be used to knockout a particular mRNA. By using lower doses to achieve efficient knockdown, the authors observe and suggest that oligo mixtures confer a distinct advantage in that they reduce the possibility of non-specific effects, since each oligo in the mixture is present in low concentration. The authors suggest that further improvements are possible by refining the mixture to eliminate non-targeting oligos.

While Wahlestedt et al. are relied on for the reasons discussed above, Wahlestedt et al. are also relied on for all they taught and reasonably suggested concerning the materials and methods for making and using LNA-containing antisense nucleic acids. To this extent, Wahlestedt et al. supplement and reinforce the teachings of Orum et al., providing yet further guidance and suggestions for designing, synthesizing, testing, and using LNA-containing

antisense nucleic acids alone or in combinations (i.e., pools, cocktails, or mixtures) as suggested by Orum et al. and Morgan et al.

While the instant references as a whole do not specifically teach placing or excluding LNA monomers in or from particular locations in an antisense molecule, such as the 5' or 3' ends, or having at least in particular 2, 4, or 5 contiguous LNA units, these variations alone are not considered to impart patentability to the claimed method in view of the prior art as represented herein which discloses both general and specific conditions for making and using a wide variety of differently modified LNA/RNA/DNA-containing nucleic acids. The positioning and percentage of each type of monomer to achieve the desired balance of cellular uptake, sequence-specific gene expression inhibition, and stability would require nothing more than routine experimentation, a matter of optimization of the chemical and physical properties and biological function that is the normal desire of any researcher. Moreover, the prior art implicitly teaches making and testing various embodiments to achieve optimal activity in a given application.

Thus, variations in the length, ratio, and placement of the LNA, DNA, and RNA segments of the oligomer, as now claimed, define nothing more than obvious variants of a class of molecule disclosed in the prior art for use in a method no different from that now claimed, which variants would reasonably be expected to be obtained during the course of routine optimization.

"Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such

concentration or temperature is critical." "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). MPEP 2144.05.II.A.

In the instant case, the prior art provides a wealth of both general and specific guidance concerning the properties and utilities of a wide variety of LNA oligomers.

"A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation." *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). MPEP 2144.05.II.B.

In the instant case, the prior art (Orum et al. and Wahlstedt et al.), by teaching the specific advantages to be achieved through the incorporation of LNA monomers in varying percentages at various positions in an antisense, provides the incentive and requisite guidance to achieve an optimum result by intentionally varying the configuration and positioning of LNA/DNA/RNA segments.

Thus, all of the claimed elements and techniques recited for use in the instant method were known in the prior art. One skilled in the art at the time of invention could have combined the elements as claimed by known methods with no change in their respective functions to yield a population of nucleic acids with predictable properties (See the U.S. Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 [82 USPQ2d 1385 (2007)]; see also *Anderson's Black Rock, Inc. v Pavement Salvage Co.* 396 U.S. 57, 163 USPQ 673 (1969)). That

is, one of skill would have predicted that LNA-containing nucleic acids of the type disclosed and suggested by Orum et al. and Wahlstedt et al., within the scope of the claimed method, could have been used in the manner taught by the prior art to inhibit gene expression to yield predictable results, and that the relative properties of such molecules would be expected to vary depending on the particular constellation of LNA/RNA/DNA segments therein.

Finally, attention is directed to *KSR Int'l Co. v. Teleflex Inc.* (550 U.S.____, 127 S. Ct. 1727 (2007)) where the Supreme Court determined that "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103 (*KSR*, 550 U.S. at ____, 82 USPQ2d at 1397)."

In the instant case the skilled practitioner would have known that antisense oligonucleotides may be of almost any length between 15 and 100 bases and could have any number of different, non-limiting percentages of LNA, DNA, and RNA monomers in various configurations and at virtually any position and that such variations would effect the hybridization kinetics, thermal stability, half-life, and Rnase H activating properties of the oligonucleotide. One of skill would have been expected to pursue the development of such antisense oligonucleotides with eye towards optimizing the activities and properties along with economic considerations involved in the manufacture of such antisense oligonucleotides.

Moreover, multi-sequence and multi-gene targeting and benefits thereof using LNA-containing oligonucleotides is taught and suggested by the prior art, as shown by Orum et al. and Morgan et al.

Accordingly, in the absent of convincing evidence to the contrary, the instantly claimed invention would have been *prima facie* obvious to one of skill in the art at the time the invention was made.

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Claims 80-83 and 157 are rejected under 35 U.S.C. 103(a) as being obvious over claims 35-44 of Birger et al. (US 2006/0147924 A1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Birger et al. disclose a method for detecting the presence of one or more target nucleic acids in a sample, said method comprising (a) incubating said sample comprising said one or

more target nucleic acids with a population of nucleic acids comprising at least one LNA oligomer, bonded to a solid support, under conditions that allow at least one of said target nucleic acids to hybridize to at least one of the nucleic acids in said population of nucleic acids. The LNA-comprising population may be any of those defined in claims 1-40, specific embodiments of which include LNAs having 2'-4' O-C methylene bridges. The term "population" as defined at page 15 of the specification therein renders obvious the embodiments specifically recited in instant claims 82 and 83.

Therefore Birger et al. taught the method as fully and intrinsically recited in the body of the claim. Cells may be considered to represent a "sample" of nucleic acids within the scope of the disclosed method.

Therefore, one of ordinary skill in the art would conclude that the invention defined in the claims at issue is anticipated by, or would have been an obvious variation of, the invention defined in the claims in the conflicting application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis V. Wollenberger whose telephone number is 571-272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louis Wollenberger/
Examiner, AU 1635
November 6, 2007